

Original quantitative research

Psychotic disorder and cannabis use: Canadian hospitalization trends, 2006–2015

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Abstract

Introduction: Given the recent and impending changes to the legal status of nonmedical cannabis use in Canada, understanding the effects of cannabis use on the health care system is important for evaluating the impact of policy change. The aim of this study was to examine pre-legalization trends in hospitalizations for mental and behavioural disorders due to the use of cannabis, according to demographic factors and clinical conditions.

Methods: We assessed the total number of inpatient hospitalizations for psychiatric conditions with a primary diagnosis of a mental or behavioural disorder due to cannabis use (ICD-10-CA code F12) from the Hospital Mental Health Database for ten years spanning 2006 to 2015, inclusive. We included hospitalizations from all provinces and territories except Quebec. Rates (per 100 000 persons) and relative proportions of hospitalizations by clinical condition, age group, sex and year are reported.

Results: Between 2006 and 2015, the rate of cannabis-related hospitalizations in Canada doubled. Of special note, however, is that hospitalizations during this time period for those with the clinical condition code “mental and behavioural disorders due to use of cannabinoids, psychotic disorder” (F12.5) tripled, accounting for almost half (48%) of all cannabis-related hospitalizations in 2015.

Conclusion: Further research is required to investigate the reasons for the increase in hospitalizations for cannabis-related psychotic disorder. The introduction of high-potency cannabinoid products and synthetic cannabinoids into the illicit market are considered as possible factors.

Keywords: *cannabis, psychotic disorders, hospitalization, Canada*

Introduction

Cannabis is a psychoactive substance widely used in Canada, with 14.8% of Canadians aged 15 years and older reporting past-year use in 2017,¹ which is comparable to the 2014 estimate of 13.2% for past-year use in the United States among Americans aged 12 years and older.² Past-year prevalence of use in Canada was higher among males (18.7%) than females (11.1%) and also among young people

aged 15 to 24 (26.9%) compared to adults aged 25 and older (12.7%).¹

Although there is evidence for moderate therapeutic effectiveness of cannabis in the treatment of some health conditions (e.g. chronic pain, chemotherapy-induced nausea and vomiting, multiple sclerosis spasticity symptoms),^{3–7} there is little evidence to suggest that cannabis can be beneficial for mental disorders and symptoms.⁸ Moreover, cannabis use, particularly

frequent use over periods of months or years, has been associated with increased risk for health harms, including psychosis,^{9–13} negative respiratory symptoms,^{12,14,15} motor vehicle collisions^{9,12,16–18} and adverse effects on adolescent brain development.^{12,19,20}

A recent study of the costs associated with substance use in Canada found that in 2014 over \$208 million was spent in cannabis-related health care costs, including over \$38 million for inpatient hospitalizations.²¹ Moreover, cannabis-related health

Highlights

- Between 2006 and 2015, the rate of hospitalizations for cannabis-related mental or behavioural disorders in Canada rose from 2.11 to 5.18 per 100 000.
- Males consistently accounted for over two-thirds of all hospitalizations for cannabis-related mental or behavioural disorders.
- Young people aged 15 to 24 years represented the greatest proportion of hospitalizations (between 49% and 58%) of any age group.
- Over the entire study period, psychotic disorder was the most common clinical condition among hospitalizations for cannabis-related mental or behavioural disorders, and accounted for 48.0% of cannabis-related hospitalizations in 2015.
- Between 2006 and 2015, the rate of hospitalizations due to cannabis-related psychotic disorder tripled, from 0.80 to 2.49 per 100 000.

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care costs have been increasing in Canada. The costs of all cannabis-attributable inpatient hospitalizations increased by 22% between 2007 and 2014,²² with the cost of inpatient hospitalizations for mental and behavioural disorders due to cannabis use increasing by 52% between 2006 and 2011.²³ As of now, there is limited research exploring the specific contribution of different mental and behavioural disorders to these observed increases in cannabis-attributable hospitalizations. This study evaluated trends in hospitalization rates between 2006 and 2015 for mental and behavioural disorders attributable to cannabis by age and sex and examined the number and proportions of these hospitalizations according to the type of clinical condition.

Methods

Data sources

Data for this analysis were acquired from the Canadian Institute for Health Information (CIHI). Specifically, data on inpatient separations (herein referred to as hospitalizations) for those with a primary diagnosis of mental and behavioural disorders due to use of cannabinoids (herein referred to as cannabis) were extracted from the Hospital Mental Health Database (HMHDB) for the ten fiscal years spanning April 2006 to March 2016 (herein referred to as 2006 to 2015). The HMHDB is a comprehensive pan-Canadian administrative database capturing demographic and clinical information on patient hospitalizations for psychiatric conditions from both general acute care and specialized psychiatric hospitals. CIHI compiles data for the HMHDB from four sources: the Discharge Abstract Database (DAD), the Hospital Morbidity Database (HMDDB), the Ontario Mental Health Reporting System (OMHRS) and the Hospital Mental Health Survey (HMHS).²⁴

Measures

Hospitalizations

We defined a hospitalization as a departure from an inpatient hospital, due to discharge or death, where the patient had a primary diagnosis of a mental or behavioural disorder due to use of cannabis. These specific diagnoses were identified using the International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Canada (ICD-10-CA), and diagnoses are determined from a patient's medical record. Given the

nature of these data, it was possible for an individual to have more than one hospital stay recorded in a given year. We included hospitalizations from all provinces and territories except Quebec. At the time of this study, data from Quebec were not available. Hospitalizations recorded in OMHRS were coded using the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV-TR), rather than the ICD-10-CA coding system, and therefore were excluded from this analysis. In any given year, a large proportion (57.3%–74.0%) of cannabis-related hospitalizations in Ontario were excluded due to being recorded in the OMHRS and coded with the DSM-IV-TR. The remainder of hospitalizations were recorded in the DAD, HMDDB or HMHS and used ICD-10-CA codes. On average, 63% of Ontario hospitalizations were excluded, meaning that a total of 1252 hospitalizations were included and 2088 hospitalizations were excluded for Ontario between 2006 and 2015.

Clinical conditions

According to ICD-10-CA, there are 10 clinical condition codes (F12.0–F12.9) used to describe the type of mental and behavioural disorder due to use of cannabis that constitutes a patient's primary reason for hospitalization. These conditions include: acute intoxication (F12.0), harmful use (F12.1), dependence syndrome (F12.2), withdrawal state (F12.3), withdrawal state with delirium (F12.4), psychotic disorder (F12.5), amnesic syndrome (F12.6), residual and late-onset psychotic disorder (F12.7), other mental and behavioural disorders (F12.8), and unspecified mental and behavioural disorder (F12.9). Full descriptions of these conditions are available from the World Health Organization.²⁵ It is important to note that none of these codes includes any information about type (plant based, extract or synthetic) or quantity of cannabis used, the route of administration (inhaled or ingested) or the reason for use (medical or nonmedical).

Age group

Counts of cannabis-related hospitalizations were categorized according to the age groups 0 to 14 years, 15 to 24 years, 25 to 44 years, 45 to 65 years and 65+ years.

Sex

Counts of cannabis-related hospitalizations were grouped by sex (male and female). Hospitalizations for which the patient's

sex was not recorded as male or female were excluded.

Analytic strategy

To examine trends in cannabis-related hospitalizations in Canada over the ten fiscal years from 2006 to 2015, we analyzed the count, proportion and sex- and age-specific rates of cannabis-related hospitalizations by year and clinical condition. Where applicable, we expressed relative proportions by clinical condition in relation to the total volume of hospitalizations for mental and behavioural disorders due to use of cannabis. We calculated the overall crude rate for the Canadian population and sex- and age-specific rates using annual population estimates derived by Statistics Canada using the mid-calendar population estimate.²⁶

In accordance with CIHI's privacy policy, at the time they provided the aggregate data requested for this analysis, some small cells were suppressed for confidentiality. This included cells with single digits (i.e. 1–9 were indicated by “\$”) as well as cells with multiple digits (i.e. 10–19 were indicated by “1\$”). For the purposes of this analysis, we replaced any suppressed digits with “1” in order to estimate hospitalizations for these cells (i.e. a cell indicated by “\$” was replaced with “1”, and a cell indicated by “1\$” was replaced with “11”).

Results

Between 2006 and 2015, the number and crude rate of hospitalizations associated with mental or behavioural disorders due to cannabis use in Canada rose from 525 (2.11 per 100 000) in 2006 to 1430 (5.18 per 100 000) in 2015 (Table 1; Figure 1).

Across all years examined, males consistently accounted for at least 70% of all cannabis-related hospitalizations and young people aged 15 to 24 years represented the greatest proportion of hospitalizations (between 49% and 58%) of any age group (Table 1).

Examination of sex- and age-specific rates for cannabis-related hospitalizations showed a 19-fold increase in hospitalization rates between 2006 and 2015 among those aged 15 to 24 years (Table 2). We also observed large increases in hospitalization rates among individuals aged 25 to 44 and individuals aged 45 to 64. Increases of

TABLE 1
Number and proportion (%) of hospitalizations for cannabis-related mental or behavioural disorders
by demographic characteristics, Canada (excluding Quebec), 2006–2015

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Overall	525	615	661	618	779	911	952	1085	1243	1430
Sex										
Male	369 (70.3)	455 (74.0)	469 (71.0)	464 (75.1)	583 (74.8)	708 (77.7)	726 (76.3)	810 (74.7)	893 (71.8)	1026 (71.7)
Female	156 (29.7)	160 (26.0)	192 (29.0)	154 (24.9)	196 (25.2)	203 (22.3)	226 (23.7)	275 (25.3)	350 (28.2)	404 (28.3)
Age										
0–14	21 ^a (4.0)	20 (3.3)	30 (4.5)	19 (3.1)	21 (2.7)	28 (3.1)	31 ^a (3.3)	22 (2.0)	30 (2.4)	41 (2.9)
15–24	272 (51.8)	302 (49.1)	353 (53.4)	341 (55.2)	428 (54.9)	486 (53.3)	503 (52.8)	627 (57.8)	691 (55.6)	746 (52.2)
25–44	178 (33.9)	229 (37.2)	211 ^a (31.9)	215 (34.8)	251 ^a (32.2)	304 (33.4)	317 (33.3)	351 (32.4)	408 (32.8)	494 (34.5)
45–64	54 (10.3)	61 ^a (9.9)	56 (8.5)	43 (7.0)	68 (8.7)	86 (9.4)	96 (10.1)	78 (7.2)	106 (8.5)	136 (9.5)
65+	1 ^a (0.2)	1 ^a (0.2)	1 ^a (0.2)	0 (0.0)	1 ^a (0.1)	7 (0.8)	1 ^a (0.1)	7 (0.6)	8 (0.6)	13 (0.9)

Data source: Canadian Institute for Health Information.²⁴

Note: Hospitalizations were extracted from the Hospital Mental Health Database (HMHDB) for the ten fiscal years spanning April 2006 to March 2016 (herein referred to as 2006 to 2015).

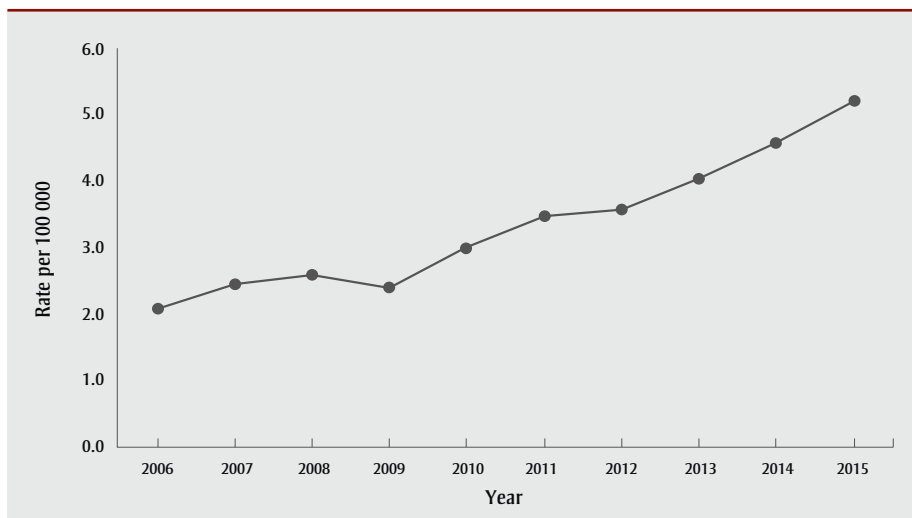
^a Estimation; small cells were suppressed to ensure confidentiality.

2.5-fold from 2006 to 2015 were reported for both males and females.

In an attempt to understand which clinical conditions might be associated with this increase, we assessed the distribution of clinical conditions for each year. In 2006, the two most common clinical conditions for cannabis-related hospitalizations—psychotic disorder and harmful use—accounted for similar proportions of hospitalizations, at 37.9% and 33.9%, respectively. However, by the end of the study period, the proportion of

hospitalizations due to cannabis-related psychotic disorder was nearly double that of hospitalizations due to harmful use of cannabis, at 48.0% and 26.0%, respectively. Throughout the course of the study, cannabis-related psychotic disorder was the most common clinical condition seen in cannabis-related hospitalizations (Figure 2). Indeed, between 2006 and 2015, the rate of hospitalizations due to cannabis-related psychotic disorder tripled, from 0.80 to 2.49 per 100 000 (data not shown).

FIGURE 1
Rate of hospitalizations for cannabis-related mental or behavioural disorder
(per 100 000) in Canada (excluding Quebec), 2006–2015



Data source: Canadian Institute of Health Information.²⁴

Note: Hospitalizations were extracted from the Hospital Mental Health Database (HMHDB) for the ten fiscal years spanning April 2006 to March 2016 (herein referred to as 2006 to 2015).

Discussion

The overall rate of cannabis-related hospitalizations increased between 2006 and 2015, with the largest increase occurring in those hospitalizations with the clinical condition code “mental and behavioural disorders due to use of cannabinoids, psychotic disorder.” These results could be due to increased prevalence of cannabis use. However, as there is little evidence for increased prevalence of cannabis use across our period of analysis, particularly among youth and young adults, we suggest that a central explanation for our results is the increasing potency of cannabis and the introduction of synthetic cannabinoids into the illicit drug market. Further, changes in the way that hospitalization data is collected and coded, as well as changes in attitudes toward reporting cannabis use, may also contribute to the observed increases in psychiatric hospitalizations.

The link between cannabis use and psychosis and schizophrenia

The link between cannabis use and the risk for developing schizophrenia is an important consideration for understanding why the largest proportions of cannabis-related hospitalizations are due to psychotic disorders. A key symptom of schizophrenia is psychosis, and a first episode of psychosis can be an initial diagnostic feature of schizophrenia, especially among those with a family history of

TABLE 2
Rates of hospitalizations for cannabis-related mental or behavioural disorders (per 100 000)
by demographic characteristics, Canada (excluding Quebec), 2006–2015

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Overall	2.11	2.44	2.59	2.40	2.99	3.46	3.57	4.02	4.55	5.18
Sex										
Male	2.98	3.64	3.71	3.63	4.51	5.43	5.49	6.05	6.59	7.50
Female	1.24	1.26	1.49	1.18	1.49	1.53	1.68	2.02	2.54	2.90
Age										
0–14	0.48 ^a	0.46	0.68	0.43	0.48	0.64	0.70 ^a	0.50	0.67	0.92
15–24	1.09	8.61	10.02	9.63	12.02	13.59	13.97	17.37	19.14	20.82
25–44	0.71	3.18	2.93 ^a	2.99	3.49 ^a	4.21	4.35	4.76	5.47	6.57
45–64	0.22	0.90 ^a	0.80	0.60	0.93	1.15	1.28	1.03	1.39	1.77
65+	0.00 ^a	0.03 ^a	0.03 ^a	0.00	0.03 ^a	0.19	0.03 ^a	0.17	0.19	0.30

Data source: Canadian Institute of Health Information.²⁴

Note: Hospitalizations were extracted from the Hospital Mental Health Database (HMHDB) for the ten fiscal years spanning April 2006 to March 2016 (herein referred to as 2006 to 2015).

^a Estimation; small cells were suppressed to ensure confidentiality.

mental disorders. Although cannabis use is significantly higher among individuals with schizophrenia,^{27,28} there is substantial evidence that cannabis use, especially frequent use over longer periods of time, increases the risk of developing both psychosis and schizophrenia.^{29–33} The risk of psychosis also increases with the frequency of cannabis use in a dose-dependent manner^{30,31,34–37} and with increasing percentage of delta-9 tetrahydrocannabinol (THC) in the product consumed.^{34–36} Early initiation of cannabis use, especially during adolescence, also elevates the risk for developing

psychotic disorders, including schizophrenia.^{38–41} Molecular genetic research demonstrates that another key factor influencing the degree of risk conferred by cannabis use for developing schizophrenia or psychosis is having a family history of these disorders.^{37,42–46} Although it has been reported that some genetic risk factors underlie both the risk for developing schizophrenia and for initiating cannabis use,^{47,48} cannabis use on its own is still an independent risk factor for psychosis and related mental disorders such as schizophrenia.

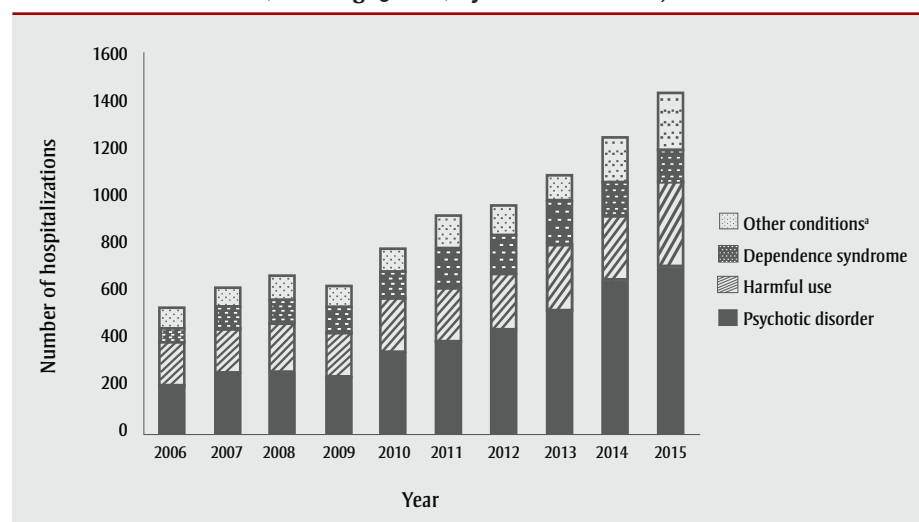
Increasing THC content in cannabis products available in the illicit market

Data from Statistics Canada show a relatively stable age of initiation among youth between 2004 and 2015,^{49–51} and that the prevalence of cannabis use actually decreased among those under the age of 25.⁵² During this same period, however, there is evidence of increased availability of high potency cannabis extracts⁵³ and the introduction of potent synthetic cannabinoids^{53–56} into the global illicit market.

Globally, the average proportion of THC, the main psychoactive component responsible for the “high” feeling associated with cannabis consumption, in herbal cannabis has risen over the last 50 to 60 years.^{53,57} While in the 1960s the proportion of THC in herbal cannabis averaged around 3%, in the early 21st century, countries have seen average proportions of THC in the range of 12% to 20%.⁵³ In addition to the increase in proportion of THC in herbal cannabis, new high-THC products referred to as “extracts” (e.g. “shatter” or “butane honey oil”) have been found with THC concentrations of 80%⁵³ to 99%.⁵⁸

Given that the use of higher potency cannabis products is associated with an increased risk of adverse health outcomes,^{25,36,53} it is possible that the increasing availability of high potency cannabis products, including herbal cannabis with higher THC potency as well as cannabis extracts, may be contributing to the increasing rate of cannabis-related hospitalizations

FIGURE 2
Number of hospitalizations for cannabis-related mental or behavioural disorders
in Canada (excluding Quebec) by clinical condition, 2006–2015



Data source: Canadian Institute of Health Information.²⁴

Note: Hospitalizations were extracted from the Hospital Mental Health Database (HMHDB) for the ten fiscal years spanning April 2006 to March 2016 (herein referred to as 2006 to 2015).

* Other conditions include acute intoxication, withdrawal state, withdrawal state with delirium, amnesic syndrome, residual/late-onset psychotic disorder, other mental and behavioural disorders and unspecified mental and behavioural disorder.

in Canada, particularly those associated with psychotic disorder.

It will be prudent to evaluate these trends from 2016 onward to the era of legalized nonmedical cannabis, and to continue to monitor them, since cannabis extracts became legal in Canada in October 2019. In addition, investments in public education and harm reduction strategies are needed to prevent hospitalizations due to cannabis use. For example, this could include increasing the awareness and implementation of the lower-risk cannabis use guidelines, which mention choosing products with lower THC content, among other recommendations, to reduce the risk of adverse health effects from cannabis.⁵⁹ The data presented here also highlight the need for comprehensive and integrated mental health and addiction services, especially for youth and young adults (i.e. aged 15–24) in order to better address the overlap between cannabis use and mental and behavioural outcomes.

Synthetic cannabinoids

Synthetic cannabinoids are a large and diverse family of compounds that, like THC, bind to cannabinoid receptors in the body, but are typically more potent and toxic.⁶⁰ Documented adverse health effects of synthetic cannabinoids include cardiovascular problems (e.g. hypertension, chest pain, tachycardia) and psychiatric issues (e.g. psychosis, anxiety, withdrawal), among others.⁶⁰ The first identification of a synthetic cannabinoid in the illicit drug supply can be traced to 2008.⁵⁵ Though there is limited Canadian epidemiological data on the use of synthetic cannabinoids, we do know that they have been used in Canada since at least 2009.⁵⁴ The 2017 Ontario Student Drug Use and Health Survey indicated that 1.5% of students in Grades 7 to 12, encompassing the ages of 12 through 18, reported using synthetic cannabis in the past year, and that this estimate had remained stable since the survey first asked about synthetic cannabinoid use in 2013.⁵⁶ Between April 2018 and April 2019, synthetic cannabinoids were found in 0.2% of samples analyzed by Health Canada's Drug Analysis Service.⁶¹ Therefore, in addition to the availability and use of higher potency cannabis products, it is also possible that the rise in cannabis-related hospitalizations may be linked to the appearance of synthetic cannabinoids in the illicit drug marketplace.

Strengths and limitations

By furthering our understanding of the clinical conditions responsible for the observed increase in cannabis-related hospitalizations, we will be in a better position to provide prevention, treatment and harm reduction strategies for those who use cannabis. Given the period of study, this analysis further provides a snapshot of hospitalization trends before legalization of nonmedical cannabis in Canada, and can be a useful benchmark to compare with post-legalization follow-up analyses.

The dataset that we analyzed only included the total number of hospitalizations and not the total number of people who were hospitalized. Therefore, we are unable to comment on the proportions of hospitalizations that may be due to a person being hospitalized multiple times throughout a fiscal year, and which conditions are associated with multiple hospitalizations. This should be an important consideration for future studies, given that 12.1% of patients hospitalized for mental illness had at least three hospital stays in 2017/18.⁶²

The dataset we used for this study was also limited as to the scope of demographic factors analyzed that could be associated with cannabis-related hospitalizations for psychiatric conditions. In addition to age and sex, important factors to consider for future studies include socioeconomic status (income and education), geography (urban vs. rural), ethnicity and the use of other substances.

The ICD-10-CA coding system used by the databases we accessed contains a great deal of detail, but there are limitations. The classification codes for mental and behavioural disorders due to use of cannabinoids do not distinguish between those admitted to hospital for disorders associated with herbal cannabis versus synthetic cannabinoids, or whether the individual admitted was using a cannabis product for medical or nonmedical purposes. Therefore, the results cannot be linked with the prevalence of use of different types of cannabis products. In addition, we cannot account for differences in clinical practice settings that may influence the ICD-10 code applied to a particular diagnosis. For example, the perceptions of health care practitioners or their awareness of cannabis as a contributor to some psychological symptoms may have changed

over time, perhaps due to increased public and political dialogue concerning cannabis legalization. The changing political landscape of cannabis throughout our period of study may also have influenced the likelihood that patients would disclose their cannabis use.

The results presented here are likely to be an underestimate of the true number of cannabis-related hospitalizations for several reasons. These data do not include inpatient hospitalizations for which a cannabis-related disorder was a secondary diagnosis. They also do not include hospitalizations for which a primary diagnosis code of “mental and behavioural disorders due to multiple drug use and use of other psychoactive substances” was given, of which some cases may be attributable to cannabis use. Further, Quebec and Ontario were not comprehensively included in the study. When investigating the clinical conditions associated with each hospital stay, only hospitalizations coded with the ICD-10-CA coding system were used, thus omitting a large proportion of cannabis-related hospitalizations in Ontario. As noted in the Methods section, approximately 63% of hospitalizations in Ontario were therefore excluded from this study's analysis. Data from Quebec, a province that accounts for close to a quarter of the Canadian population, were not available for this analysis. Finally, we applied conservative estimation procedures for dealing with suppressed data cells, since these were assumed to have a value of 1, despite the actual value ranging between 0 and 9 due to secondary data suppression.

Conclusion

The increasing rate of hospitalizations due to cannabis-related psychotic disorder in Canada between 2006 and 2015 is a trend that warrants further investigation, in light of both what is known regarding the association between frequent cannabis use and psychosis and the recent legalization of nonmedical cannabis use in Canada. Further research is required to clarify the cause of these increased harms, particularly among those with the highest rate of cannabis-related hospitalizations (younger individuals and males), in order to better target public education efforts around lower-risk use and prevention of cannabis-related harms. Ongoing monitoring of cannabis use and related harms, including high potency cannabis products such as cannabis extracts and synthetic

cannabinoids, will also be essential to understanding the impact of legislative change on these trends in the future.

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Conflicts of interest

The authors have no conflicts of interest to declare.

Authors' contributions and statement

All four authors, BMH, SCW, SK and MMY, contributed to each stage of developing the manuscript. This includes the research design, acquisition of data, analysis of data, drafting and revising of the paper, and approval of the final manuscript.

The content and views expressed in this article are those of the authors and do not necessarily reflect those of the Government of Canada.

References

- Government of Canada. Canadian Tobacco, Alcohol and Drugs (CTADS) Survey: 2017 detailed tables [Internet]. Table 13: Illegal drug use (past-12-month and lifetime), by age group and sex, 2017. Ottawa (ON): Government of Canada; 2018 [updated 2019 Jan 04; cited 2019 Jan 23]. Available from: <https://www.canada.ca/en/health-canada/services/canadian-tobacco-alcohol-drugs-survey/2017-summary/2017-detailed-tables.html>
- Azofeifa A, Mattson ME, Schauer G, et al. National estimates of marijuana use and related indicators – National Survey on Drug Use and Health, United States, 2002–2014. *MMWR Morb Mortal Wkly Rep*. 2016;65(No. SS-11):1-25.
- National Academies of Sciences, Engineering, and Medicine. The health effects of cannabis and cannabinoids: the current state of evidence and recommendations for research. Washington (DC): The National Academies Press; 2017.
- Andrae MH, Carter GM, Shaparin N, et al. Inhaled cannabis for chronic neuropathic pain: a meta-analysis of individual patient data. *J Pain*. 2015; 16(12):1221-32.
- Whiting PF, Wolff RF, Deshpande S, et al. Cannabinoids for medical use: a systematic review and meta-analysis. *JAMA*. 2015;313(24):2456-73.
- Smith LA, Azariah F, Lavender VT, et al. Cannabinoids for nausea and vomiting in adults with cancer receiving chemotherapy. *Cochrane Database Syst Rev*. 2015(11): CD009464.
- Koppel BS, Brust JC, Fife T, et al. Systematic review: efficacy and safety of medical marijuana in selected neurologic disorders: report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology*. 2014;82(17):1556-63.
- Black N, Stockings E, Campbell G, et al. Cannabinoids for the treatment of mental disorders and symptoms of mental disorders: a systematic review and meta-analysis. *Lancet Psychiatry*. 2019;6(12):995-1010.
- Hall W. What has research over the past two decades revealed about the adverse health effects of recreational cannabis use? *Addiction*. 2015;110(1): 19-35.
- Moore TH, Zammit S, Lingford-Hughes A, et al. Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. *Lancet*. 2007;370(9584):319-28.
- Marconi A, Di Forti M, Lewis CM, et al. Meta-analysis of the association between the level of cannabis use and risk of psychosis. *Schizophr Bull*. 2016;42(5):1262-9.
- Volkow ND, Baler RD, Compton WM, et al. Adverse health effects of marijuana use. *N Engl J Med*. 2014; 370(23):2219-27.
- Konefal S, Gabrys R, Porath A. Clearing the smoke on cannabis: regular use and mental health. Ottawa (ON): Canadian Centre on Substance Use and Addiction; 2019. 18 p.
- Tashkin DP. Effects of marijuana smoking on the lung. *Ann Am Thorac Soc*. 2013;10(3):239-47.
- Tetraault JM, Crothers K, Moore BA, et al. Effects of marijuana smoking on pulmonary function and respiratory complications: a systematic review. *Arch Intern Med*. 2007;167(3):221-8.
- Asbridge M, Hayden JA, Cartwright JL. Acute cannabis consumption and motor vehicle collision risk: systematic review of observational studies and meta-analysis. *BMJ [Internet]*. 2012 [cited 2018 Jun];344:e536. doi: 10.1136/bmj.e536.
- Hartman RL, Huestis MA. Cannabis effects on driving skills. *Clin Chem*. 2013;59(3):478-92.
- Li M-C, Brady JE, DiMaggio CJ, et al. Marijuana use and motor vehicle crashes. *Epidemiol Rev*. 2011;34(1): 65-72.
- Lubman DI, Cheetham A, Yücel M. Cannabis and adolescent brain development. *Pharmacol Ther*. 2015;148: 1-16.
- Jager G, Ramsey NF. Long-term consequences of adolescent cannabis exposure on the development of cognition, brain structure and function: an overview of animal and human research. *Curr Drug Abuse Rev*. 2008;1(2): 114-23.
- Canadian Substance Use Costs and Harms Scientific Working Group. Canadian substance use costs and harms (2007–2014). (Prepared by the Canadian Institute for Substance Use Research and the Canadian Centre on Substance Use and Addiction.) Ottawa (ON): Canadian Centre on Substance Use and Addiction; 2018. 54 p.
- Canadian Substance Use Costs and Harms Scientific Working Group. Canadian substance use costs and harms visualization tool, version 1.0.0 [Online tool]. Ottawa (ON): Canadian Centre on Substance Use and Addiction and the Canadian Institute for Substance Use Research; 2019 [cited 2019 May 23]. Available from: <https://csuch.ca/explore-the-data/>
- Young MM, Jesseman RJ. The impact of substance use disorders on hospital use. Ottawa (ON): Canadian Centre on Substance Abuse; 2014. 31 p.

24. Canadian Institute for Health Information. Hospital Mental Health Database, 2015-2016. Ottawa (ON): Canadian Institute for Health Information; 2017.
25. World Health Organization. International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10)-WHO Version: 2016. Geneva (CH): World Health Organization; 2016. Available from: <http://apps.who.int/classifications/icd10/browse/2016/en#/F12>
26. Statistics Canada. Table 051-001: Estimates of population, by age group and sex for July 1, Canada, province and territories [Internet]. Ottawa (ON): Statistics Canada; 2019 [cited 2019 Apr 11]. Available from: <https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1710000501>
27. Hunt GE, Large MM, Cleary M, et al. Prevalence of comorbid substance use in schizophrenia spectrum disorders in community and clinical settings, 1990–2017: systematic review and meta-analysis. *Drug Alcohol Depend.* 2018;191:234-58.
28. McLoughlin BC, Pushpa-Rajah JA, Gillies D, et al. Cannabis and schizophrenia. *Cochrane Database Syst Rev.* 2014;10:CD004837.
29. Gage SH, Jones HJ, Burgess S, et al. Assessing causality in associations between cannabis use and schizophrenia risk: a two-sample Mendelian randomization study. *Psychol Med.* 2017;47(5):971-80.
30. Marconi A, Di Forti M, Lewis CM, et al. Meta-analysis of the association between the level of cannabis use and risk of psychosis. *Schizophr Bull.* 2016;42(5):1262-9.
31. Moore TH, Zammit S, Lingford-Hughes A, et al. Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. *Lancet.* 2007;370(9584):319-28.
32. Myles N, Newall H, Nielssen O, et al. The association between cannabis use and earlier age at onset of schizophrenia and other psychoses: meta-analysis of possible confounding factors. *Curr Pharm Des.* 2012;18(32):5055-69.
33. National Academies of Sciences, Engineering, and Medicine. The health effects of cannabis and cannabinoids: the current state of evidence and recommendations for research. Washington (DC): National Academies Press; 2017. 486 p.
34. Di Forti M, Marconi A, Carra E, et al. Proportion of patients in south London with first-episode psychosis attributable to use of high potency cannabis: a case-control study. *Lancet Psychiatry.* 2015;2(3):233-8.
35. Di Forti M, Morgan C, Dazzan P, et al. High-potency cannabis and the risk of psychosis. *Br J Psychiatry.* 2009;195(6):488-91.
36. Di Forti M, Sallis H, Allegrì F, et al. Daily use, especially of high-potency cannabis, drives the earlier onset of psychosis in cannabis users. *Schizophr Bull.* 2014;40(6):1509-17.
37. Karcher NR, Barch DM, Demers CH, et al. Genetic predisposition vs. individual-specific processes in the association between psychotic-like experiences and cannabis use. *JAMA Psychiatry.* 2019;76(1):87-94.
38. Arseneault L, Cannon M, Poulton R, et al. Cannabis use in adolescence and risk for adult psychosis: longitudinal prospective study. *BMJ.* 2002;325(7374):1212-13.
39. Hanna RC, Perez JM, Ghose S. Cannabis and development of dual diagnoses: a literature review. *Am J Drug Alcohol Abuse.* 2017;43(4):442-55.
40. Hosseini S, Oremus M. The effect of age of initiation of cannabis use on psychosis, depression, and anxiety among youth under 25 years. *Can J Psychiatry.* 2019;64(5):304-12.
41. Levine A, Clemenza K, Rynn M, et al. Evidence for the risks and consequences of adolescent cannabis exposure. *J Am Acad Child Adolesc Psychiatry.* 2017;56(3):214-25.
42. Caspi A, Moffitt TE, Cannon M, et al. Moderation of the effect of adolescent-onset cannabis use on adult psychosis by a functional polymorphism in the catechol-O-methyltransferase gene: longitudinal evidence of a gene X environment interaction. *Biol Psychiatry.* 2005;57(10):1117-27.
43. Colizzi M, Iyegbe C, Powell J, et al. Interaction between functional genetic variation of DRD2 and cannabis use on risk of psychosis. *Schizophr Bull.* 2015;41(5):1171-82.
44. Estrada G, Fatjó-Vilas M, Muñoz M, et al. Cannabis use and age at onset of psychosis: further evidence of interaction with COMT Val158Met polymorphism. *Acta Psychiatr Scand.* 2011;123(6):485-92.
45. Lodhi RJ, Wang Y, Rossolatos D, et al. Investigation of the COMT Val158Met variant association with age of onset of psychosis, adjusting for cannabis use. *Brain Behav [Internet].* 2017 [cited 2018 Jun];7(11):e00850. Available from: <https://onlinelibrary.wiley.com/doi/epdf/10.1002/brb3.850>
46. Pelayo-Terán JM, Pérez-Iglesias R, Mata I, et al. Catechol-O-Methyltransferase (COMT) Val158Met variations and cannabis use in first-episode non-affective psychosis: clinical-onset implications. *Psychiatry Res.* 2010;179(3):291-6.
47. Power RA, Verweij KJ, Zuhair M, et al. Genetic predisposition to schizophrenia associated with increased use of cannabis. *Mol Psychiatry.* 2014;19(11):1201-4.
48. Verweij KJ, Abdellaoui A, Nivard MG, et al. Short communication: genetic association between schizophrenia and cannabis use. *Drug Alcohol Depend.* 2017;171:117-21.
49. Statistics Canada. Canadian Tobacco Use Monitoring Survey (CTUMS) 2012: supplementary tables [Internet]. Ottawa (ON): Statistics Canada; 2013 [modified 2013 Oct 1; cited 2018 Jun]. Available from: <https://www.canada.ca/en/health-canada/services/publications/healthy-living/canadian-tobacco-use-monitoring-survey-2012-supplementary-tables.html>
50. Statistics Canada. Canadian Tobacco, Alcohol and Drugs Survey for 2013 [public-use microdata file]. Ottawa (ON): Statistics Canada; 2015.
51. Statistics Canada. Canadian Tobacco, Alcohol and Drugs Survey for 2015 [public-use microdata file]. Ottawa (ON): Statistics Canada; 2017.

52. Rotermann M, Macdonald R. Analysis of trends in the prevalence of cannabis use in Canada, 1985 to 2015. *Health Rep.* 2018;29(2):10-20.
53. Murray RM, Quigley H, Quattrone D, et al. Traditional marijuana, high-potency cannabis and synthetic cannabinoids: increasing risk for psychosis. *World Psychiatry.* 2016;15(3):195-204.
54. Canadian Community Epidemiology Network on Drug Use. Synthetic cannabinoids in Canada [CCENDU Bulletin]. Ottawa (ON): Canadian Centre on Substance Abuse; 2014 Mar. 5 p.
55. European Monitoring Centre for Drugs and Drug Addiction. Perspectives on drugs: synthetic cannabinoids in Europe. Lisbon (Portugal): European Monitoring Centre for Drugs and Drug Addiction; 2017. 9 p.
56. Boak A, Hamilton HA, Adlaf EM, Mann RE. Drug use among Ontario students, 1977–2017: detailed findings from the Ontario Student Drug Use and Health Survey (CAMH Research Document Series No. 46). Toronto (ON): Centre for Addiction and Mental Health; 2017. 341 p.
57. ElSohly MA, Mehmedic Z, Foster S, et al. Changes in cannabis potency over the last 2 decades (1995–2014): analysis of current data in the United States. *Biol Psychiatry.* 2016;79(7):613-9.
58. Canadian Centre on Substance Use and Addiction. Edible cannabis, cannabis extracts and cannabis topicals: a primer on the new cannabis products. Ottawa (ON): Canadian Centre on Substance Use and Addiction; 2019. 2 p.
59. Fischer B, Russell C, Sabioni P, et al. Lower-risk cannabis use guidelines (LRCUG): a comprehensive update of evidence and recommendations. *Am J Public Health.* 2017;107(8):e1-e12.
60. Antoniou T, Juurlink DN. Synthetic cannabinoids. *CMAJ.* 2014;186(3):210.
61. Drug Analysis Service. DAS Data SAD 04-2018 to 04-2019 [data file]. Ottawa (ON): Health Canada; 2019.
62. Canadian Institute for Health Information. Repeat hospital stays for mental illness [Internet]. Ottawa (ON): Canadian Institute for Health Research; 2019 [cited 2019 Oct 30]. Available from: <https://yourhealthsystem.cihi.ca/hsp/inbrief?lang=en#!/indicators/007/repeat-hospital-stays-for-mental-illness;/mapC1;mapLevel2/>